

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Additionally, claims 20-41 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 20, 25, 28-30 and 38 stand rejected under 35 U.S.C. §102(a) as anticipated by NCBI ENTREZ ACCESSION NO: gi:100473.

Claims 20-26, 28-30 and 38 stand rejected under 35 U.S.C. §102(b) as anticipated by NCBI ENTREZ ACCESSION NO: gi:1931504.

## II. Response to the Rejection of Claims 20 and 30-41 Under 35 U.S.C. §112, First Paragraph

The US Patent and Trademark Office ("the Patent Office") rejected claims 20 and 30-41 "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *Official Action*, page 2-3. Applicants respectfully traverse the rejection and submit the following comments.

Initially, applicants note that, with respect to the written description requirement of 35 U.S.C. §112, first paragraph, it is the Patent Office's burden to establish a *prima facie* case of unpatentability with respect to applicants' presumptively adequate written description. ("As in cases involving the enablement requirement of § 112 . . . we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims" (*In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976)). Applicants submit that in the present case the Patent Office has not demonstrated that one of ordinary skill in the art would not conclude that applicants have possession of the claimed invention described in the specification as filed and therefore that the Patent Office has not met this burden.

It appears that the Patent Office is basing its rejection of claims 20 and 30-41 on its contention that the present specification does not "set forth an explicit or implicit description of a nucleic acid sequence that meets the limitation of 'capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(f)' or 'having a nucleotide

sequence at least 70% identical to a sequence provided in claim 20 and that does not encode the polypeptide set forth as SEQ ID NO:2". *Official Action*, page 4. Applicants note, however, that courts have repeatedly held that the question of whether the written description requirement is met depends on what a person of ordinary skill in the art would understand, based on consideration of the specification, and not on the explicit disclosure of particular embodiments. See, e.g., *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000); *In re Hayes Microcomputer Prods., Inc.*, 982 F.2d 1527, 25 U.S.P.Q.2d 1241 (Fed. Cir. 1992).

Continuing, applicants note that the *Guidelines for Examination of Patent Applications Under the 35 USC 112, §1 "Written Description" Requirement* ("the Guidelines") indicate that the written description requirement can be satisfied by "sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure of relevant, identifying characteristics." *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, §1 "Written Description" Requirement*, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001). See also, *University of California v. Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) and *MPEP* §2163.II.A.ii.

Applicants submit that the specification as filed discloses an extensive list of representative species and relevant characteristics of the species, thereby satisfying the written description requirement of 35 U.S.C. §112, first paragraph. Particularly, applicants direct attention to pages 34-39 of the specification, wherein an extensive list of N-terminal and C-terminal deletion polypeptides are disclosed. The specification states "polynucleotide sequences encoding these polypeptides are also provided" (*Specification*, page 35, lines 26-27, and page 37, lines 4-5). These deletion polypeptides are fragments of the nucleic acid and polypeptide sequences of SEQ ID NOs:1 and 2. Additional discussion of polynucleotide and polypeptide fragments can be found in the section of the specification beginning on page 64. These polynucleotide sequences (a) would be expected to hybridize under stringent conditions (which are described in the specification, for example on page 15, line 15-34 and page 46 through page 49, line 28, including Table 2 presented therein) to the polynucleotides specified in (a)-(f) of claim 20, (b) have a nucleotide sequence that is at least 70% identical to a sequence provided in claim 20; and (c) do not encode the polypeptide set forth as SEQ ID NO:2. Therefore, the amino acid and/or polynucleotide sequences are representative of the claimed genus.

Applicants further note that in addition to the disclosed N- and C-terminal deletion polynucleotides, the specification describes the use of conservative substitutions in generating variants of the polynucleotides and polypeptides of the present invention (page 60, line 35-page 63, line 35, including Table 3 presented therein). Such variants can have a different sequence from that of SEQ ID NO:2, yet retain the properties recited in claim 20. Thus, this group of variants highlights yet more species that are representative of the claimed genus.

With respect to the characteristics of these members of the claimed genus, applicants submit that the description of the features of SEQ ID NOs:1 and 2 is itself a recitation of the relevant identifying characteristics common to the members of the genus, because the members included within the genus will be encoded by a variant of SEQ ID NO:1 and will share the features of the reference sequence (e.g., 70% identity with the reference sequence, capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(f) of claim 20 and/or encoding at least 50 contiguous amino acids of SEQ ID NO:2). In other words, the identifying characteristics of the members of the genus are those of the reference sequence (i.e., SEQ ID NOs:1 and/or 2). One of ordinary skill in the art, upon consideration of SEQ ID NO:2 and the specification of the present application, would readily appreciate a range of particular proteins (i.e., species) that would be representative of the genus of claim 20. Thus, the representative members of the genus are distinguished from others by various identifying features, namely the features of the reference sequence.

Next, applicants draw attention to the statement that "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosures necessary to satisfy the written description requirement." *Guidelines for Examination of Patent Applications Under the 35 USC 112, ¶1 "Written Description" Requirement*, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001). The Patent Office has identified the relative level of skill in the pertinent field as "very high." *Official Action*, page 9. Therefore, applicants submit that given the high level of skill in the field identified by the Patent Office, the large number of species representative of the claimed genus disclosed in the present specification, coupled with the discussion of their relevant identifying characteristics, the invention is fully described in accordance with 35 U.S.C. §112, first paragraph.

Applicants submit that, in view of (a) the extensive disclosure of N- and C-terminal deletion polypeptides and the polynucleotides that encode these polypeptides, presented in the

specification, (b) the disclosure of species comprising conservative substitutions of SEQ ID NO:2, (c) the recitation of identifying characteristics of the members of the claimed genus, and (d) the high level of skill in the art, claims 20 and 30-41 are in accord with the Guidelines and the pertinent case law (see, e.g., *University of California v. Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997)), and that the written description requirement of 35 U.S.C. §112, first paragraph, has been met. Summarily, applicants submit that one of ordinary skill in the art would recognize that applicants had invented what was claimed, which is the standard against which the adequacy of a written description is gauged. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). Accordingly, applicants respectfully request that the rejection of claims 20 and 30-41 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn. Applicants further submit that claims 20 and 30-41 are in condition for allowance and respectfully solicit the same.

### III. Response to the Rejection of Claims 20-41 Under 35 U.S.C. §112, First Paragraph

The Patent Office rejected claims 20-41 under 35 U.S.C., §112 first paragraph "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." *Official Action*, page 6. Summarily, it is the Patent Office's position that "given no more than the teachings available in the specification and prior art, the skilled artisan would have to resort to trial and error experimentation to establish the function of the claimed polypeptide before experiments to develop diagnostics or therapeutics could even be contemplated. This amount of experimentation would clearly be undue." *Official Action*, page 10. Applicants respectfully traverse the rejection and submit the following comments.

It is initially noted that as a matter of Patent Office practice, the burden rests upon the Patent Office to establish a *prima facie* case of a failure to comply with 35 U.S.C. § 112, first paragraph, with respect to the invention described and claimed in applicants' presumptively enabling patent application. *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1971), *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976). More specifically, the Patent Office bears the burden of establishing by a preponderance of evidence that one of ordinary skill in the art would not be enabled to practice the present invention after considering the present disclosure in combination with what is known in the art.

Applicants respectfully submit that in its formulation of the rejection of claims 20-41 under 35 U.S.C. §112, first paragraph, the Patent Office has adopted an inappropriate standard for measuring enablement. More particularly, it appears that the Patent Office has not given due weight what is known in the art. The appropriate standard is that the claimed invention must be enabled so that a person skilled in the art can make and use the invention from the disclosures of the present U.S. patent application, coupled with information known in the art, without "undue experimentation." *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988).

It is applicants' position that the Patent Office has failed to give due weight to what is known to those of ordinary skill in the art when it formulated its rejections under 35 U.S.C. §112, first paragraph. Applicants again note that the Patent Office's burden is to demonstrate that the disclosure combined with what is known in the art does not enable one of ordinary skill in the art to practice the invention commensurate with the scope of the claims. Applicants submit that although the Patent Office has presented a general discussion of pertinent factors involved in making an enablement analysis, the Patent Office has not provided any concrete evidence that one of ordinary skill in the art would not be enabled by the present disclosure, combined with what is known in the art, to employ the compositions and methods of the present disclosure.

Furthermore, it appears that the Patent Office is requiring that applicants submit working examples in order to comply with the requirements of 35 U.S.C. §112, first paragraph. However, no such requirement is recited by the statute or the applicable case law. While the presence or absence of working examples can be a consideration in the overall evaluation of enablement, working examples are not required under 35 U.S.C. §112, first paragraph, to comply with the enablement standard presented therein. Indeed, the M.P.E.P. states that the U.S. patent application need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *M.P.E.P.* §2164.02. The M.P.E.P. also states that a lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement. *Id.* (emphasis added). Thus, there does not appear to be any evidentiary support for the rejection of claims 20-41 under 35 U.S.C. §112, first paragraph with respect to enablement.

Contrary to the Patent Office's position, the specification of the present invention provides guidance sufficient to practice the present invention as claimed. The specification provides guidance for cloning the polynucleotides of the present invention (e.g., page 211, Example 3), expressing the polypeptides of the present invention (e.g., page 229, Example 14), performing various bioinformatic analyses (e.g., page 210, Example 1), identifying the presence of an abnormal level of a polypeptide of the present invention (e.g., page 252, Example 24) and tissue profiling (e.g., page 213, Example 4), to name just a few examples. Clearly, relevant experimental procedures and conditions are disclosed and applicants submit that in consideration of the level of skill in the art and the scope of claims 20-41, the specification is fully enabling. Applicants submit that given the knowledge of what is known in the pertinent art (e.g., standard molecular biological and/or biochemical laboratory techniques), one of ordinary skill in the art would be fully enabled by the present disclosure.

Turning to the Patent Office's assessment of the level of experimentation required to practice the claimed invention, it is applicants' position that, even if it might require considerable experimentation to develop diagnostics or therapeutics using the claimed polynucleotides, the quantity of experimentation to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 195 U.S.P.Q. 150, 153 (C.C.P.A. 1977). "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the U.S. patent application in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed." *In re Wands*, 8 U.S.P.Q.2d at 1404 (citing *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976)).

Thus, although some degree of experimentation might be required in order to develop diagnostics or therapeutics, the specification of the present disclosure provides guidelines for such a procedure. By following the guidance provided in the present disclosure, one of ordinary skill in the art would be able to develop a diagnostic protocol and/or therapeutics. No experimentation is required, beyond routine parametric optimization protocols, a process well known to those of skill in the art. Accordingly, applicants respectfully request that the rejection of these claims under 35 U.S.C. §112, first paragraph, be withdrawn and the subject claims allowed.

Applicants further submit the following comments. With respect to the enablement requirement of 35 U.S.C. §112, first paragraph, the Patent Office has summarized its position as follows: "[t]he issue at hand, therefore, is whether the skilled artisan would be able, provided the teachings of the specification and prior art, to develop diagnostics or therapeutics using the claimed polynucleotides without undue experimentation." *Official Action*, page 7. The Patent Office argues that in order to use the claimed polynucleotides a skilled artisan must identify the activity of the polynucleotides or encoded polypeptides, correlate that activity with a disease state and develop diagnostics or therapeutics from the claimed polypeptides. *Official Action*, page 7.

Focusing on claims 20-41 of the present invention, the Patent Office contends these claims are not enabled because undue experimentation would be required to develop therapeutics using the claimed polynucleotides and/or polypeptides. Applicants note, however, that although the polynucleotides and/or polypeptides of the present invention might be useful as a therapeutic or in the development of a therapeutic, this function of the polypeptides and polynucleotides of the present invention is not claimed in claims 20-41 and uses for the sequences other than as a therapeutic are presented in the specification. Applicants note that courts have established that a claimed invention need not accomplish all objectives stated in the specification; only one is necessary. *Raytheon Company v. Roper Corporation*, 724 F.2d 951, 220 U.S.P.Q. 592 (Fed. Cir. 1983). In its opinion, the *Raytheon* court stated, "requiring that all claims must set forth inventions satisfying all objectives would make no sense." *Raytheon* at 958. In the present case, the specification need only enable a person of ordinary skill in the art to make the claimed polynucleotides and polypeptides and practice a single use of the claimed polynucleotide and polypeptide sequences without undue experimentation.

Applicants submit that the specification of the present invention fully describes the isolation of the polynucleotide sequence of SEQ ID NO:1, and also discloses the production of a polypeptide of SEQ ID NO:2, encoded by SEQ ID NO:1. Methods of producing and isolating such a polypeptide are also provided in the specification as filed. Thus, the question then becomes whether the specification describes an application for the claimed polynucleotides and polypeptides, which need not necessarily be a therapeutic, such that one of ordinary skill in the art would be able to practice the application.

Continuing, applicants now direct attention to Example 19 on page 238 of the specification as filed wherein a description of antibody formation is presented, as well as to pages 71-101 of the specification, which also presents an extensive discussion of antibody formation. Attention is further directed to pages 101-113 wherein various uses for the formed antibodies are described, including detailed guidance in using antibodies generated in accordance with the present invention in immunophenotyping, in assays for antibody binding, in therapeutic uses of antibodies and in antibody-based gene therapy.

Additionally, applicants present a method of determining alterations in a gene corresponding to a polynucleotide in Example 23 on page 251 of the specification as filed. In another embodiment, Example 24, on pages 252-253 of the specification as filed describes a method of detecting abnormal levels of a polypeptide in a biological sample. In yet another embodiment, Example 31 on pages 273-275 describes a method of generating of a transgenic animal. All of these applications employ the sequences of the present invention and all of the applications are described to a level at which one of ordinary skill in the art could practice them. Applicants therefore submit that in view of the disclosure of the sequences, a discussion of methods of preparing the sequences and a discussion of methods of using the sequences in a variety of applications, claims 20-41 meet the enablement requirement of 35 U.S.C. §112, first paragraph.

Applicants recognize that claim 34 is directed to a method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject. However, the claim recites the use of the polynucleotide of claim 20, which, as noted above, is extensively described in the specification, including methods of isolating and preparing such a polynucleotide. Thus, one of ordinary skill in the art would readily be able to use such a polynucleotide in the method of claim 34, upon consideration of the guidance provided in the specification (see, e.g., page 180, line 26 to page 181, line 20). For example, a condition associated with the NF- $\kappa$ B pathway, with which the polypeptides and polynucleotides of the present invention were associated (page 215, Example 6), or inflammatory diseases including rheumatoid arthritis, asthma, multiple sclerosis, osteoarthritis (page 22).

Applicants further note that in addition to describing methods of determining identity in the specification, claim 38 specifically recites the use of a CLUSTALW global sequence alignment. A detailed description of the nature and use of the CLUSTALW alignment is



provided in the specification on pages 53, line 30 to page 55, line 25. Thus, one of ordinary skill in the art is provided with yet more guidance with which to practice the claimed invention.

Applicants therefore submit that in consideration of the discussion of the features and preparation of the polynucleotides and polypeptides of the present invention provided in the specification, as well as the high level of skill in the pertinent art, and the guidance the specification provides in a range of applications for the sequences of the present invention, claims 20-41 are fully enabled.

Applicants submit that claims 20-41 are in full compliance with 35 U.S.C. §112, first paragraph, and respectfully request that the rejection of claims 20-41 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn. Applicants further submit that claims 20-41 are in condition for allowance and respectfully solicit the same.

#### IV. Response to the Rejection of Claims 20, 25, 28-30 and 38 Under 35 U.S.C. §102(a)

The Patent Office has rejected claims 20, 25, 28-30 and 38 under 35 U.S.C. §102(a) as anticipated by NCBI ENTREZ ACCESSION NO: gi:100473. Applicants respectfully traverse the rejection and submit the following comments.

Initially, applicants wish to note that in the Official Action, the Patent Office refers to gi:100473. Applicants believe the Patent Office intended to refer to gi:10039473, indicated on the NCBI printout and alignment supplied by the Patent Office, rather than gi:100473. Therefore, the following comments are directed to the sequence referenced as gi:10039473.

It is well settled that for a cited reference to qualify as prior art under 35 U.S.C. §102, each element of the claimed invention must be disclosed within the reference. "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Upon careful consideration and review of gi:10039473, applicants respectfully submit that the disclosure of gi:10039473 does not disclose each and every element of the present invention. Specifically, gi:10039473 does not disclose the complete sequence of SEQ ID NO:2.

More particularly, gi:10039473 does not disclose the first 12 amino acids of SEQ ID NO:2. Therefore, since the cited sequence is shorter than SEQ ID NO:2, it cannot anticipate SEQ ID NO:2. Analogously, a polynucleotide encoding SEQ ID NO:2 (e.g., SEQ ID NO:1)

cannot be anticipated by gi:10039473, because gi:10039473 does not encode the full sequence of SEQ ID NO:2.

Applicants additionally note that gi:10039473 is an unannotated chromosomal sequence. The scope of the present invention, however, encompasses only isolated sequences and sequences that have been altered by the hand of man (i.e., an isolated nucleic acid sequence that exists in a form not found in nature). Explicitly excluded are chromosomal sequences. Applicants direct attention to page 13, lines 5-17 of the specification as filed, wherein applicants state:

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

Applicants therefore submit that, since genomic DNA is explicitly excluded from the scope of claims 20-26, 28-30 and 38 of the present invention by the recitation of the term "isolated" therein, gi:10039473 does not anticipate claims 20-26, 28-30 and 38 of the present application. Bearing in mind the patent law tenet "[t]hat which would literally infringe if later in time anticipates if earlier than the date of invention" (*Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747, 3 USPQ2d 1766, 1768 (Fed. Cir. 1987)), applicants submit that since the use of gi:10039473 would not infringe claims 20, 25, 28-30 and 38 (because it is specifically excluded from the scope of the present invention), gi:10039473 cannot anticipate claims 20, 25, 28-30 and 38.

In summary, applicants submit that gi:10039473 does not disclose an isolated polynucleotide sequence encoding SEQ ID NO:2 of the present invention. Therefore, applicants submit that gi:10039473 does not anticipate claims 20, 25, 28-30 and 38 of the present invention. Applicants therefore respectfully request that the rejection of these claims under 35 U.S.C. §102(a) be reconsidered and withdrawn. Applicants further submit that claims 20, 25, 28-30 and 38 are in condition for allowance and respectfully solicit the same.

V. Response to the Rejection of Claims 20-26, 28-30 and 38 Under 35 U.S.C. §102(b)

The Patent Office has rejected claims 20-26, 28-30 and 38 under 35 U.S.C. §102(b) as anticipated by NCBI ENTREZ ACCESSION NO: gi:1931504. Applicants respectfully traverse the rejection and submit the following comments.

Applicants initially note that it appears the Examiner has mistakenly referred to NCBI ENTREZ ACCESSION NO: gi:1931504 in the text of the Official Action, but included an alignment of NCBI ENTREZ ACCESSION NO:gi:2133864. Applicants therefore assume that the Examiner intended to cite NCBI ENTREZ ACCESSION NO:gi:2133864 in his rejection under 35 U.S.C. §102(b). The following remarks, therefore are directed to SEQ ID NO:2 of the present invention in view of NCBI ENTREZ ACCESSION NO:gi:2133864.

Applicants again note that for a cited reference to qualify as prior art under 35 U.S.C. §102, each element of the claimed invention must be disclosed within the reference. Upon careful consideration and review of gi:1931504, applicants respectfully submit that the disclosure of gi:1931504 does not anticipate the claims of the present application under 35 USC 102(b).

The remarks presented above with respect to gi:10039473 are equally applicable to sequence gi:2133864. Restating and summarizing, applicants note that gi:2133864 is an unannotated chromosomal sequence. The claims of the present invention, on the other hand, encompass only isolated sequences, that is, sequences that have been altered by the hand of man, based on the definition provided in the specification for the term "isolated." Explicitly excluded are chromosomal sequences. Thus, gi:2133864 cannot anticipate claims 20-26, 28-30 and 38 because it is a chromosomal sequence (and not "isolated"), which has been excluded from the scope of the claims in question.

Applicants submit that gi:2133864 does not anticipate the isolated polynucleotides as claimed in claims 20-26, 28-30 and 38 of the present invention. Applicants therefore respectfully request that the rejection of claims 20-26, 28-30 and 38 under 35 U.S.C. §102(b) be reconsidered and withdrawn. Applicants further submit that claims 20-26, 28-30 and 38 are in condition for allowance and respectfully solicit the same.

## VI. Conclusions

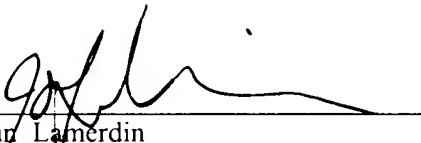
In light of the above amendments and remarks, applicants submit that the subject patent application is in condition for allowance and courteously solicit a Notice of Allowance.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

Although it is believed no additional fee is due, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment associated with the filing of this correspondence to Deposit Account Number 19-3880.

Respectfully submitted,

Bristol-Myers Squibb Company  
Patent Department  
P.O. Box 4000  
Princeton, NJ 08543-4000  
(609) 252-3575  
Date: March 18, 2003

  
\_\_\_\_\_  
John Lamerdin  
Attorney for Applicants  
Reg. No. 44,858